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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,073	07/17/2007	Yves Claude Nicolau	ACI-0403US	4203

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EXAMINER
KIM, YUNSOO

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
01/06/2012	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,073	NICOLAU ET AL.	
	Examiner	Art Unit	
	YUNSOO KIM	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2011*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *19,20,23,25,26,28-32* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *19,20,23,25,26 and 28-32* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/22/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 19, 20, 23, 25, 26 and 28-32 are pending upon entry of Applicant's amendment filed on 11/7/11.

Since a prior art revealed no prior art on SEQ ID NO:5, the search has extended to include SEQ ID NO:1.

2. Applicants' submission of IDS filed on 11/22/11 has been acknowledged.

3. In light of Applicant's amendment to the claims filed on 11/7/11, the rejection under 35 U.S.C. 112, first paragraph (new matter, see sections 11-13 of the office action mailed on 7/6/11).

4. The following rejections remain. In light of Applicant's amendments to the claims, the rejection is modified to reflect the issues of current claim set filed on 11/7/11.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 19, 20, 23, 25, 26 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of restoring memory and curiosity awakening by administering supramolecular antigenic construct comprising an antigenic peptide set forth in SEQ ID NO:1-6 with palmitoylation and pegylation, does not reasonably provide enablement for methods to restoring memory and curiosity awakening by administering any supramolecular antigenic constructs comprising any active fragments of amyloid or any peptides of GXXXGXXXGG or GXXXG motifs.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed.Cir.1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of the skilled in the art to practice the claimed invention.

The claimed is drawn to the method of improving pathological conditions (e.g. memory restoration and curiosity awakening) of Alzheimer's disease comprising administering a supramolecular constructs of any GXXXGXXXGG or GXXXG peptide motifs and the construct may be used in treating disorders comprising Alzheimer's disease. Wolf-Klein et al teaches that there is no medical treatment currently available to cure of stop the progression of Alzheimer's disease (Wolf-Klein et al., Am Journal of Hosp Palliat Care, 2007, 24(1):77-82, abstract, in particular, of record) despite of current pharmaceutical advances in delaying disease progression. Even though there are five FDA approved Alzheimer's drugs, they temporarily relieve some symptoms of the diseases. Further, Wolf-Klein et al. discloses that the length of survival has not changed despite new technology and therapeutic approaches and the tolls of this incurable disease continue to increase (abstract, p. 77, 2nd col.)

In addition, Applicants have not provided any *in vivo* working examples that the supramolecular constructs with fragments Aβ peptides and peptides of GXXXGXXXGG or GXXXG motifs can be used in methods of restoring memory and curiosity awakening.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed supramolecular constructs in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of

enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicant's response and amendments to the claims filed on 11/7/11 have been fully considered but they were not persuasive.

Applicant has asserted that the restoring of memory by administration of supramolecular constructs of amyloid peptides are known in the art and Applicant has referenced Muhs et al. (PNAS, 2007, vol. 104, p. 9810-9815).

As Applicant has acknowledged, Muhs et al. discloses efficacy of liposomal based vaccine comprising the amyloid peptide 1-15 (Aβ1-15). The prior art peptide is relevant to support the claimed SEQ ID NO:1-6 but does not support any active fragments of Aβ peptides or peptides having GXXXGXXXGG or GXXXG motifs.

Contrary to Applicant's assertion, the claimed invention is not limited to restore memory and curiosity awakening by administration of supramolecular construct having the SEQ ID NO:1-6 rather the claimed method encompasses other unspecified fragments of Aβ peptides and GXXXGXXXGG or GXXXG peptide motifs. As discussed above, Wolf-Klein et al teaches that there is no medical treatment currently available to cure or stop the progression of Alzheimer's disease (Wolf-Klein et al., Am Journal of Hosp Palliat Care, 2007, 24(1):77-82, abstract, in particular, of record) despite of current pharmaceutical advances in delaying disease progression. Even though there are five FDA approved Alzheimer's drugs, they temporarily relieve some symptoms of the

diseases. Further, Wolf-Klein et al. discloses that the length of survival has not changed despite new technology and therapeutic approaches and the tolls of this incurable disease continue to increase (abstract, p. 77, 2nd col.). Moreover, the specification of the instant application in p. 3 acknowledges that the delaying and reversing the progression is largely unsuccessful. The specification of the instant application states:

> The management of AD consists of medication-based and non-medication based treatments. Treatments aimed at changing the underlying course of the diseases (delaying or reversing the progression) have so far been largely unsuccessful.

For the reasons addressed previously, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed supramolecular constructs in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. Claims 19, 20, 23, 25, 26 and 28-32 are rejected under 35. U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of supramolecular antigenic constructs wherein the antigenic construct is a SEQ ID NOs:1-6 with a modification such as palmitoylation; however, Applicant is not in possession of any supramolecular antigenic constructs comprising any

unspecified amyloid peptide motifs including GXXXG and GXXXGXXXGG or any fragments thereof.

The claims broadly encompass any peptides from any amyloid proteins in any lengths. The specification does not provide written description for such broad genus peptide encompassed by the claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The guidelines of the Examination of Patent Applications Under the 35 U.S.C. 112 § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e.., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Fri. January 5, 2001, see especially page 1106, column 3).

The antigenic peptide of the instant claims is drawn to any peptide that is obtained from any amyloid protein and some may have GXXXG and GXXXGXXXGG motifs. The specification of the instant application discloses some peptides (as in claim 25) that are derived from Aβ amyloid. However, the claimed peptide is not limited to Aβ amyloid but encompasses any amyloid proteins and the fragments thereof. It is noted that amyloid

is defined as any complex protein that is deposited in tissues and shares selected laboratory features such as a change in the fluorescence intensity of certain aromatic dyes (Medicine Net definition, 8/8/04, of record) and there are number of other amyloids does not have any structural relationship with Aβ amyloid (wikipedia, 2009, p. 1-6, of record). Given that the broad range of peptides is claimed, it is apparent that the instant specification fails to disclose any species of peptides that are non Aβ amyloid. Thus, the failure of disclosure is not sufficiently representative of the broad genus of structurally different antigenic peptides other than Aβ amyloid sequences of claim 25.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant's arguments filed on 11/7/11 have been fully considered but they were not persuasive.

Applicant has asserted that the current claim amendment obviates the rejection as the antigenic fragments are SEQ ID NOs:1-5 and this satisfies the representative number of species..

Contrary to Applicant's assertion, the claimed peptide is not limited to β amyloid or fragments set forth in the SEQ ID NOs:1-6 but includes any antigenic polypeptide that encompassed by any fragments of β amyloid and other unspecified amino acid sequences in addition to the β amyloid sequence and the sequences encompassed by the GXXXG and GXXXGXXXGG motifs. Given that the broad range of peptides is claimed, it is

apparent that the instant specification fails to disclose any species of antigenic peptides that comprise any fragments of β amyloid and unspecified amino acids or structural motifs set by GXXXG and GXXXGXXXGG other than SEQ ID NO:1-6. Thus, the failure of disclosure is not sufficiently representative of the broad genus of structurally different antigenic peptides other than β amyloid sequences of claim 25.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 19, 20, 23, 25, 26 and 28-32 stand rejected under 35 U.S.C. 102(b) as being anticipated by Nicolau et al. (PNAS, 2002 vol. 99, no. 4, p. 2332-2337, IDS reference, of record) for the reasons set forth in the office action mailed on 7/6/11.

Nicolau et al. teach administration of antigenic composition comprising a peptide comprising the claimed SEQ ID NO:1 in a reconstituted liposome comprising phospholipids and cholesterol (Fig.1, p. 2333) in PBS (e.g. pharmaceutical carrier). Further, Nicolau et al. teach that a hydrophobic (e.g. palmitoylic acid) tail is attached to a lysine residue of the peptide (Introduction, p. 2332) and the peptide is derived from Aβ amyloid sequence.

Claims 28-30 are included in this rejection because the SEQ ID NO:1 has GXXXG and GXXXGXXXGG motifs as is evidenced by the specification of the instant application in p. 25-26.

Given that the identical antigenic composition is administered to a group of subject having Aβ plaques (p. 2333, col. 2), the referenced composition inherently enhances the antigenicity in a patient of Alzheimer's disease.

Even if the claimed method does not recite a particular patient population, the patient population having Aβ plaques cannot be excluded from the study because having Aβ plaques is considered as indication of Alzheimer's disease (p. 2332). Thus, prior art population and the potential population of the claimed method are considered identical. Therefore, the reference teachings anticipate the claimed invention.

Applicant's arguments filed on 11/7/11 have been fully considered but they were not persuasive.

For clarification purpose, the rejection is under 35 U.S.C. 102 (b) – note Applicant has addressed 102(a) in the response filed on 11/7/11 (p.11).

Applicant has asserted that the Nicolau et al. is not a proper anticipatory reference as the reference fails to teach memory restoration and curiosity awakening and this is not enabling by the Nicolau reference (p. 11 of the response filed on 11/7/11 based on p.2337 of Nicolau). The current claim set recites the method for "restoring memory and curiosity awakening" and Applicant has addressed that this is an important therapeutic effect on the brain during the telephonic interview held on 10/27/11.

Applicant has further asserted that the Nicolau et al. express serious doubt to the NOBRA mouse model in the treatment of Alzheimer's diseases because the NOBRA model does not provide a blood-brain barrier to cross for the antibodies to reach the pancreatic plaques. Applicant has traversed that the Nicolau et al. do not provide any evidence that the antigenic structures for clearing plaques from the brain based *in vitro* data of Fig 4.

Contrary to Applicant's assertion, the currently claimed construct used in the claimed method and the prior art construct are identical. Given that the identical composition to the claimed invention is being administered to the same patient population, the administration of the composition will inherently achieve the intended purpose of the claimed invention - restore memory restoration and curiosity awakening.

However, it is noted that the structure of the claimed invention can be differentiated from the prior art structure. As disclosed in specification in p. 22 of the instant application, the claimed invention may be further described to add peg moieties in addition to the palmitoylation of in the lysine residue of the structure of the Nicolau reference. This distinction may be critical to support the currently amended intended use of the supramolecular construct in restoring memory and curiosity awakening by crossing the blood-brain barrier while the construct lacking the pegylation may not able to achieve such functions.

As the currently amended claims do not specify the structural differences between the claimed supramolecular construct and the prior art construct (both recite antigenic peptide and hydrophobic moieties), the claimed supramolecular construct would inherently achieve the intended use of the claimed method. Therefore, the reference teachings anticipate the claimed invention and the rejection is maintained.

10. The following new ground of rejection is necessitated by Applicant's amendment filed on 11/7/11.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 29-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The specification or the original claims as filed does not provide a written description the phrase "wherein a portion of the β-amyloid fragment consist of" of claims 29-30 and

"hydrophobic moieties are fatty acids, triglycerides or phospholipids" as in claim 31, respectively. Applicant has not specified where the support comes from for claims 29 and 30. It is noted that the specification in p. 25 discloses that the motifs are for the entire β-amyloid (1-42) and does not support for any portion thereof. Moreover, the asserted passage of p.15-16 is for claim 32 of the specific carbon lengths but it does not provide written support for genuses of fatty acids, triglycerides or phospholipids recited in claim 31.

The instant claims now recite a limitation which was not clearly disclosed in the specification as filed, and now changes the scope of instant disclosure as filed.

Such limitations recited in the present claims, which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C.112.

13. No claims are allowable.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to YUNSOO KIM whose telephone number is (571)272-3176. The examiner can normally be reached on M-F,9-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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January 5, 2012

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